

The Use of High Throughput Experimentation In Catalyst Research

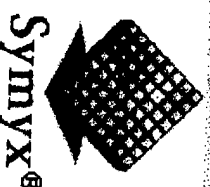
J. C. Stevens, R. Rosen

The Dow Chemical Company
Freeport, TX

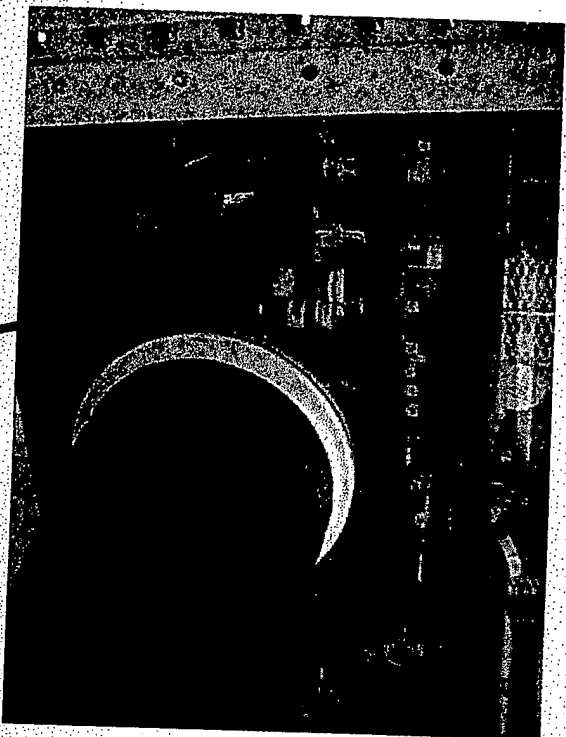
T. Boussie, G. Diamond, C. Goh, K. Hall, A. M. LaPointe, M. Leclerc,
C. Lund, V. Murphy, J. Shoemaker, H. Turner, U. Tracht, T. Uno

Symyx Technologies
Santa Clara, CA

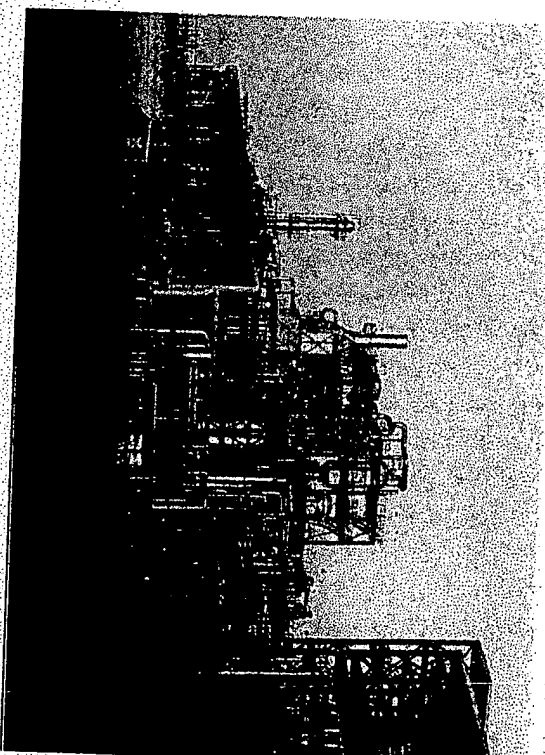
FLEXP0 2002



New Polyolefin Catalysts Drive New Business Growth



From this



To this

The Rate of New Product Creation Has Been Faster With Single-Site Catalysts

HDPE
(L)LDPE

- PP

- EPDM

Plastomers (AFFINITY™, Exact™, Luflexen™)

Ethylene/norbornene elastomers (NORDEL-IP™)

Ethylene/octene elastomers (ENGAGE™)

Ethylene/styrene interpolymers (INDEX™)

- Elastomeric/soft PP homopolymers (EHPP, FPO)

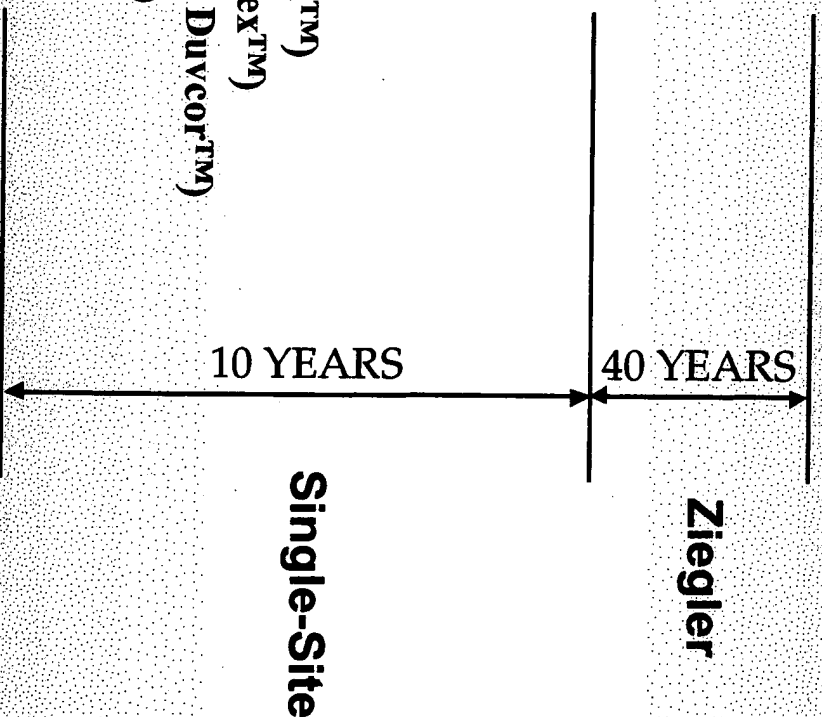
Liquid polyolefins (Trilene™, Paramins™, Versipol™)

Ethylene/CO copols. (polyketones Carilon™, Ketonex™)

Poly(substituted)norbornene (Avatrell™, Appearl™, Duvcor™)

Ethylene/cyclic olefin copolymers (Topas™, Apel™)

Syndiotactic polystyrene (QUESTRA™, Xarec™)



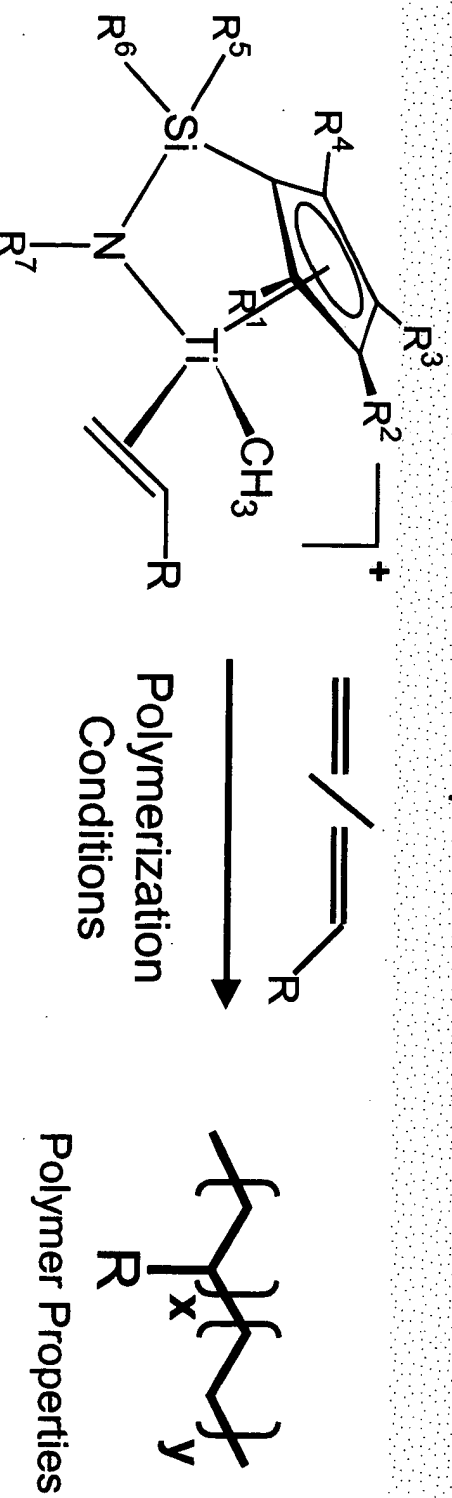
Rate of New Market Creation. Source: STA* research

Single-Site Catalyst Discovery Research Centers On :

- ❖ **More Productive Catalysts**
- ❖ **Higher Temperature Operation**
- ❖ **Higher Molecular Weights**
- ❖ **Higher Comonomer Contents**
- ❖ **Improved / Novel Control of Sequence Distributions**
- ❖ **Incorporation of New Comonomers**
- ❖ **Improved / Differentiated Products**
- ❖ **Novel Polymer Microstructures and Tacticity**

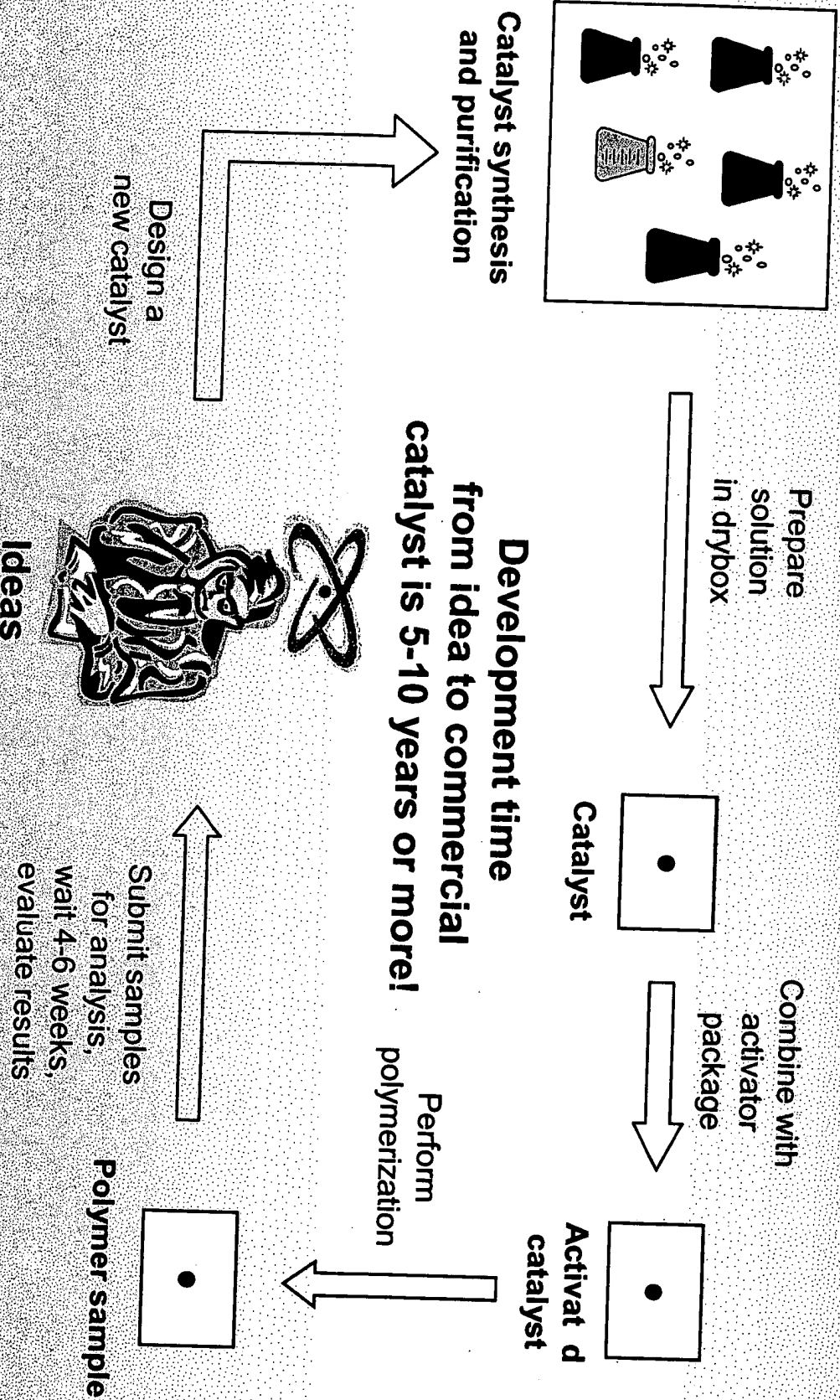
Complete Evaluation of the Structure / Activity Relationships for any Catalyst Family is a Daunting Task

The Energy Surface for a Copolymerization is Highly Complex

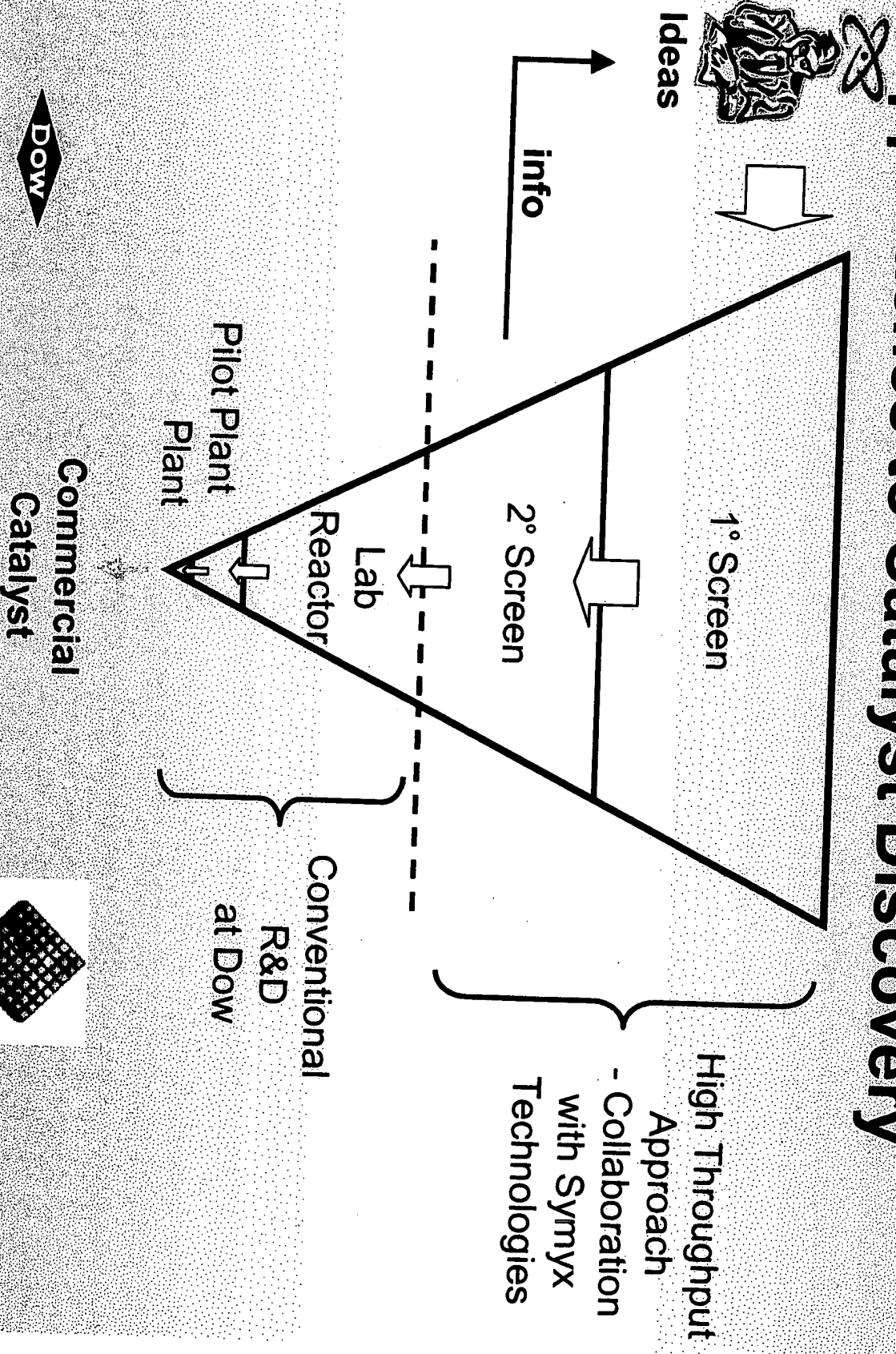


- 1) Properties of active site and polymer can be affected *dramatically and unpredictably* by variations in choice of Metal, Ligand(s), Activation Method and Process Conditions
- 2) Choosing Ten Substituents for Each Position on this ligand Generates around 10,000,000 Compounds !!!

The Conventional Way of Doing Catalyst R&D is Effective But Can Be Slow



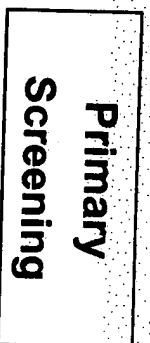
Combinatorial and High-Throughput Approaches to Catalyst Discovery



Experimental Throughput of Synyx / Dow Collaboration

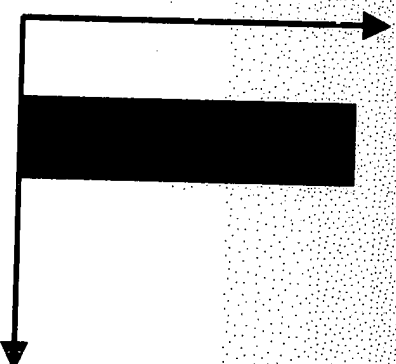
“Discovery Screening”

High Throughput
Lower Precision
Yes/No Approach



-----> 500

Experiments per Day



Hits and Information

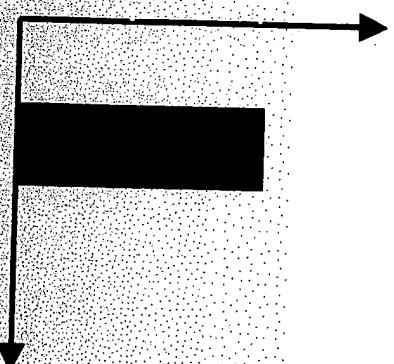
“Optimization Screening”

Moderate Throughput
Higher Precision



-----> 100

50



“Experiment” means catalyst synthesis, polymerization, and analysis of performance, polymer properties, etc.

High Throughput Catalyst Discovery Requires:

Large Number of Ligands with Suitable Diversity

Efficient Methods of Attaching Ligands to Metals

Comprehensive Activation Strategies

High Throughput **Primary** Screen

- Rapid analytical for activity, molecular weight, at smaller scales

High Throughput **Secondary** Screen

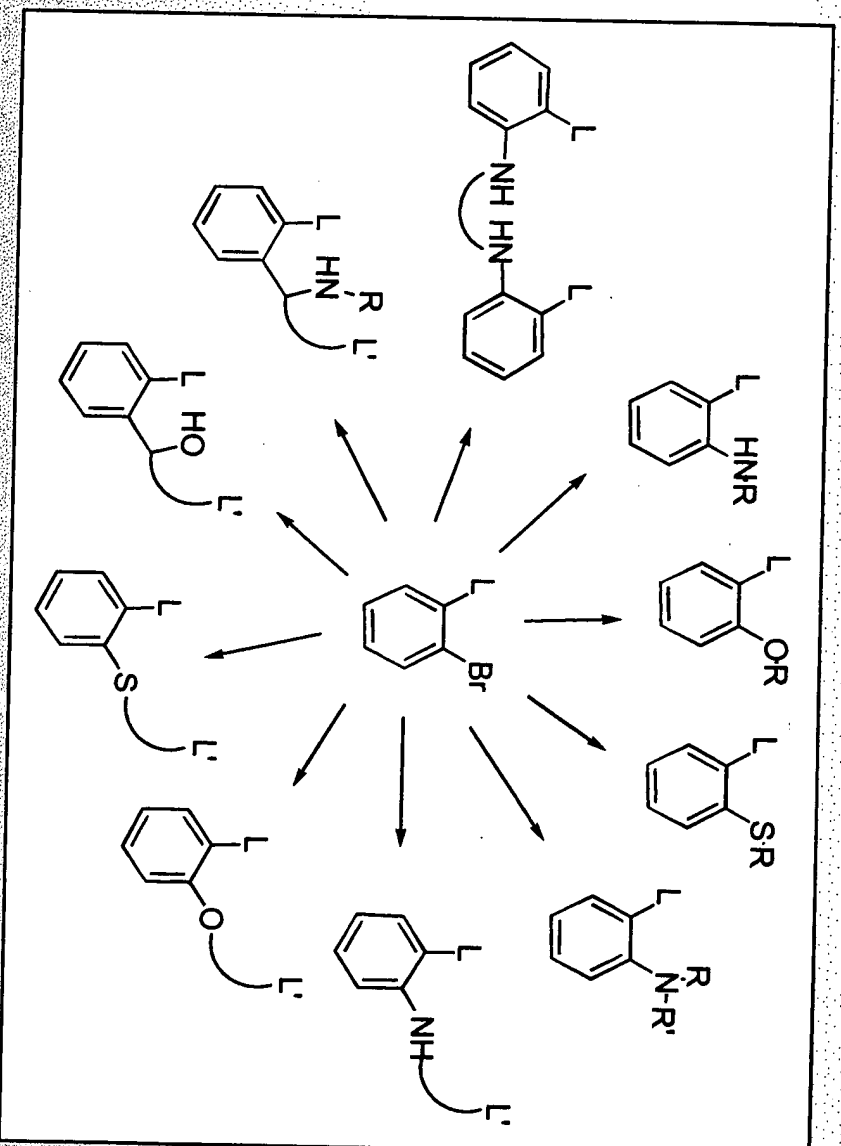
- Rapid analytical for activity, molecular weight, MWD, comonomer incorporation, tacticity, etc

Ligand Diversity: The Building Block Strategy

How can we exploit parallel synthesis techniques to create *diverse* ligand libraries?

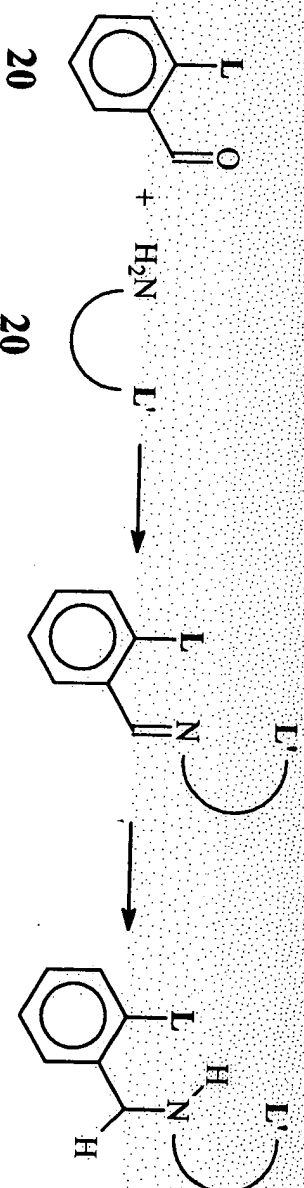
- Focus on post-metallocene catalyst systems
- Create diverse functionalized building blocks
- Connect building blocks using high-yield coupling reactions

The Parallel Building-Block Approach Leads To Significant Diversity:

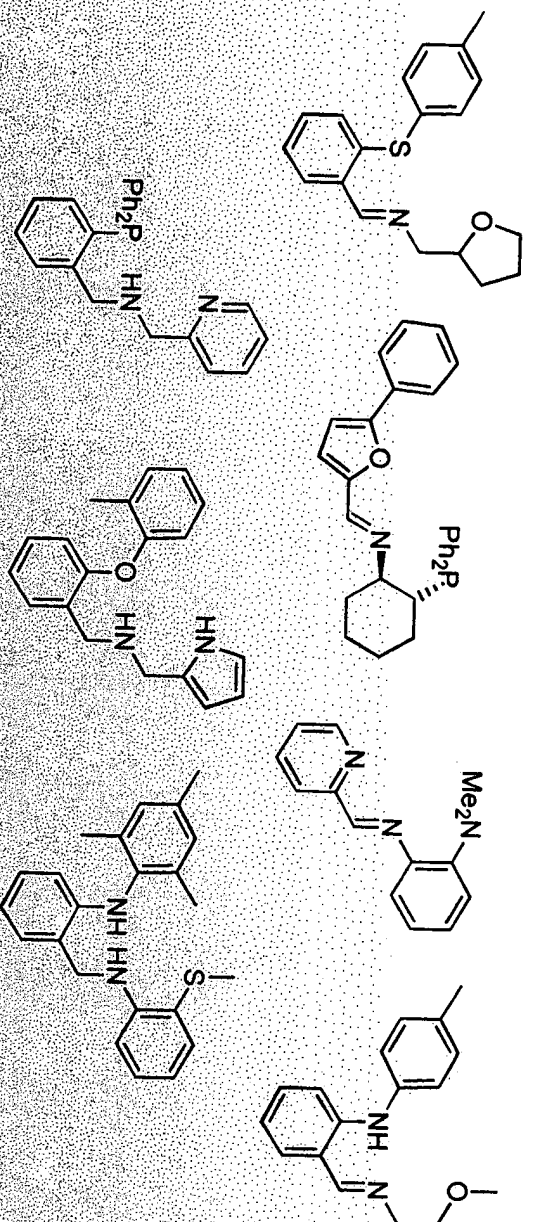


One Example of Ligand Diversity via General Transformations

imine Condensation/Reduction:



20 x 20 x 2 = 800 Examples !!



800 ligands x 6 metals x 3
monomers x 5 activators x
3 temperatures = 216,000
experiments!

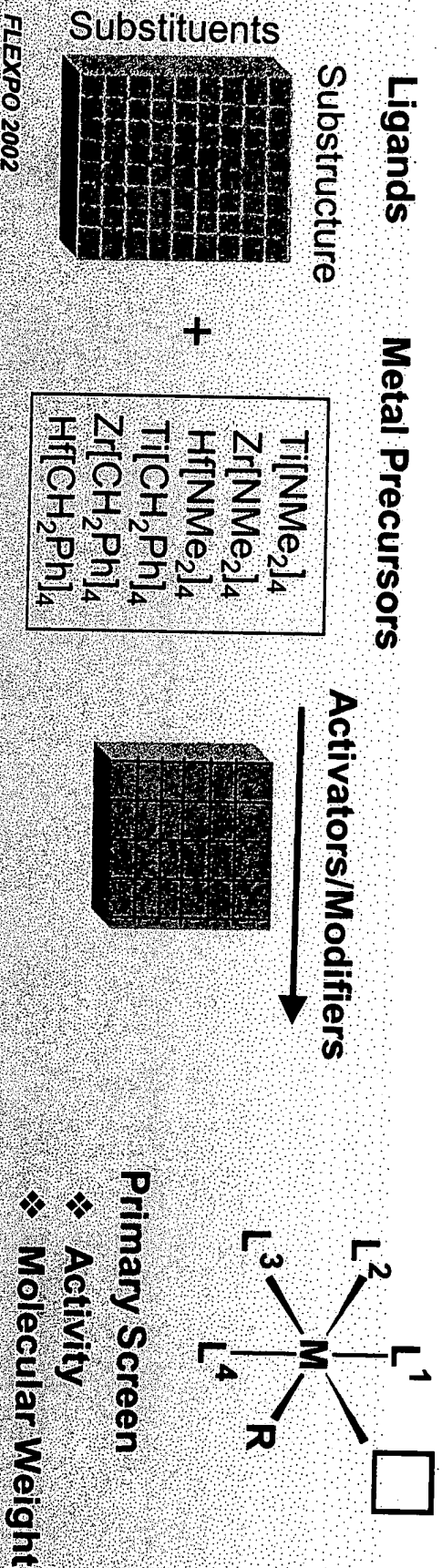
Issues With Parallel Synthesis of Activated Metal Complexes

How can I rapidly ...

- Synthesize a diverse set of organometallic compounds, and
- know what I made, and
- select the appropriate activator?

By ...

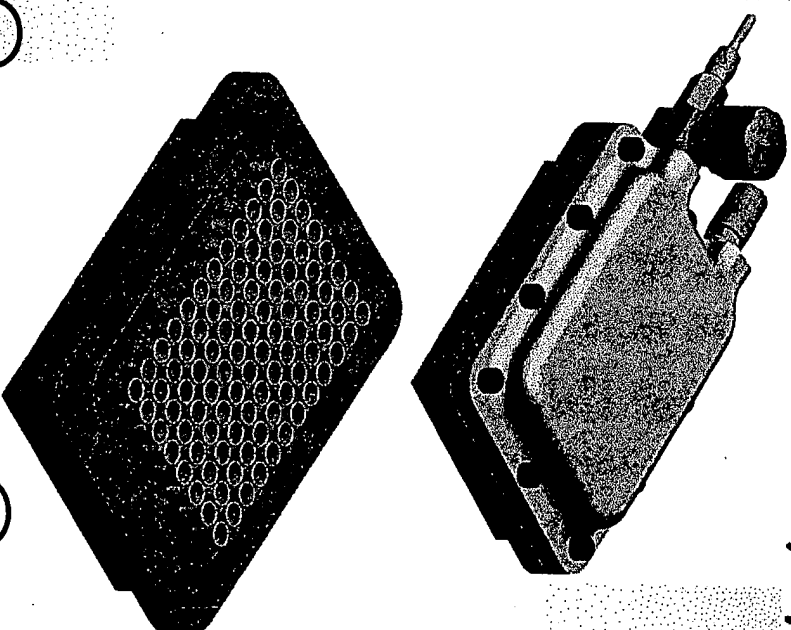
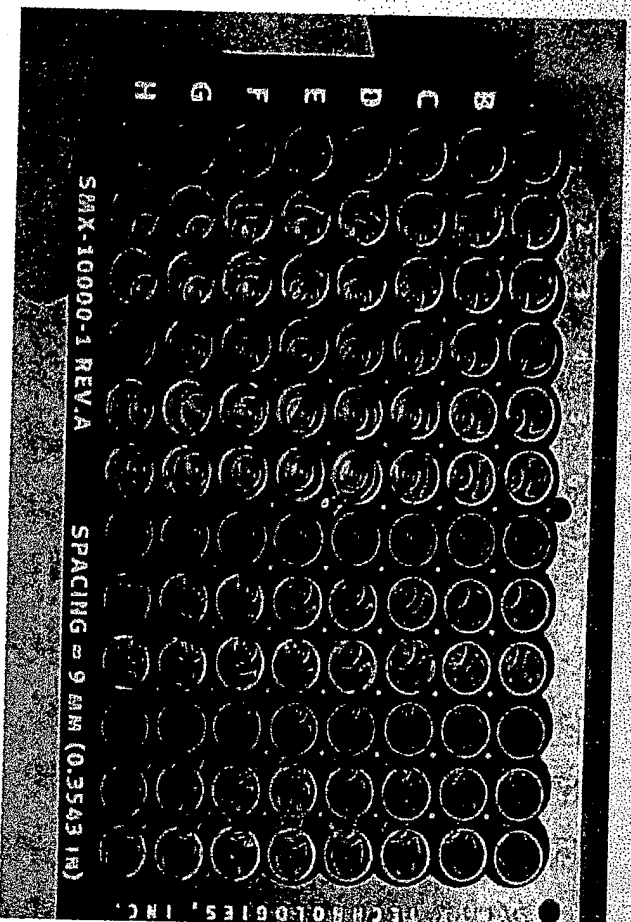
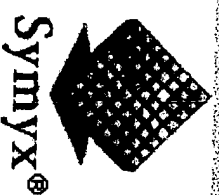
- accommodating multiple organometallic routes, and
- multiple activation chemistries for each metal / ligand set, and
- validating chemistry with models before experiment and for all hits



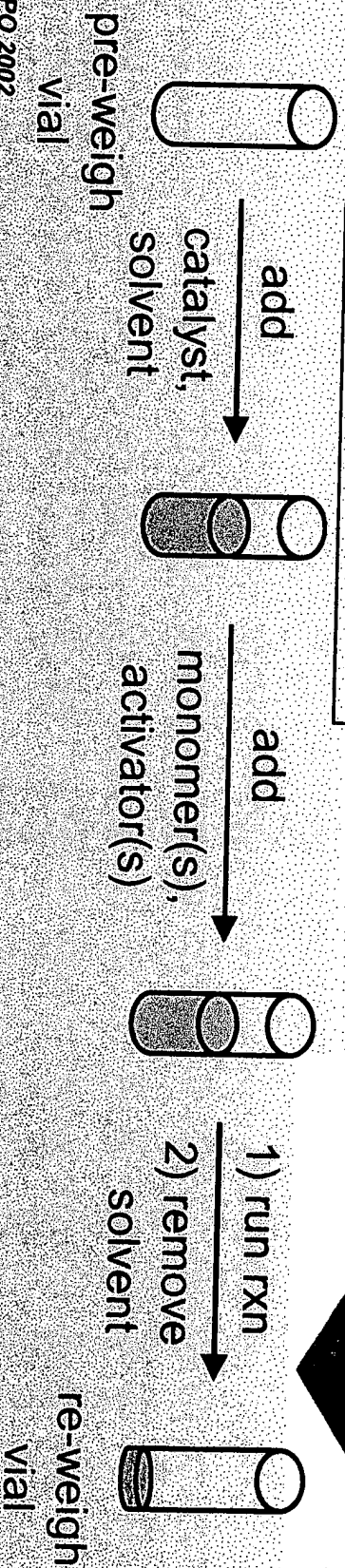
FILEXPO 2002



Rapid Primary Screen Using Post Reaction Gravimetric Analysis



All Procedures Employ
Robotic Liquid Handling

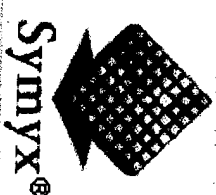
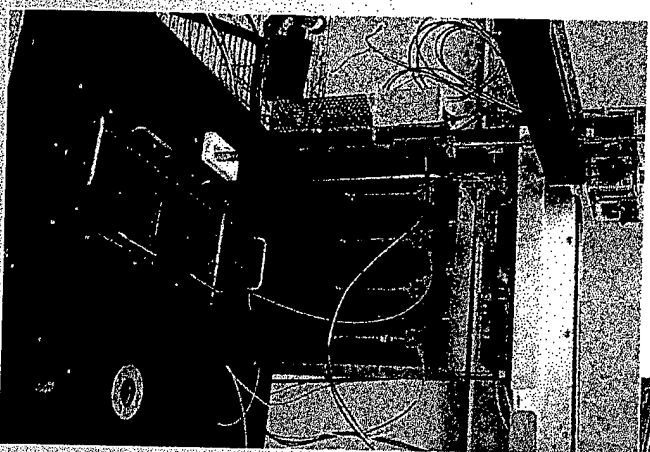


FLEXPO 2002



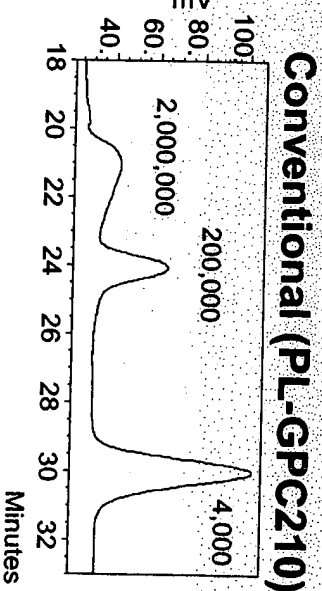
High-Throughput Molecular Weight Measurements

Symyx Rapid GPC™

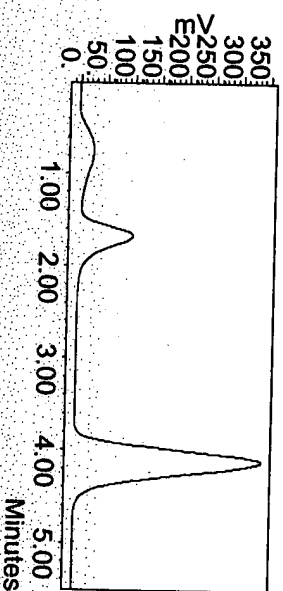


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Conventional: ≥ 80
40 min/sample



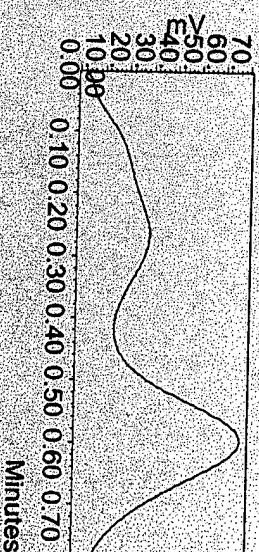
High Resolution



6 Minutes

90 Seconds

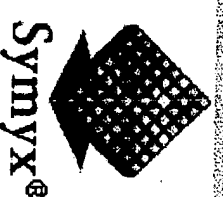
High Throughput



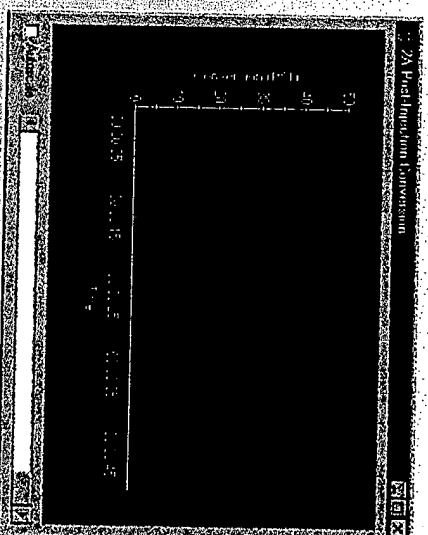
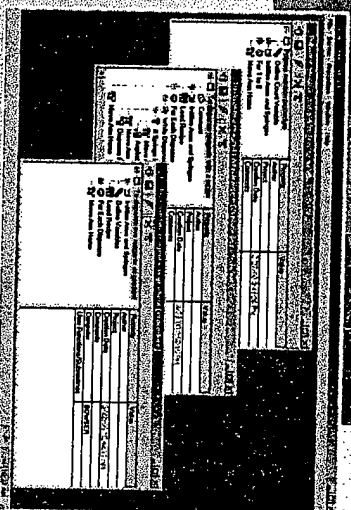
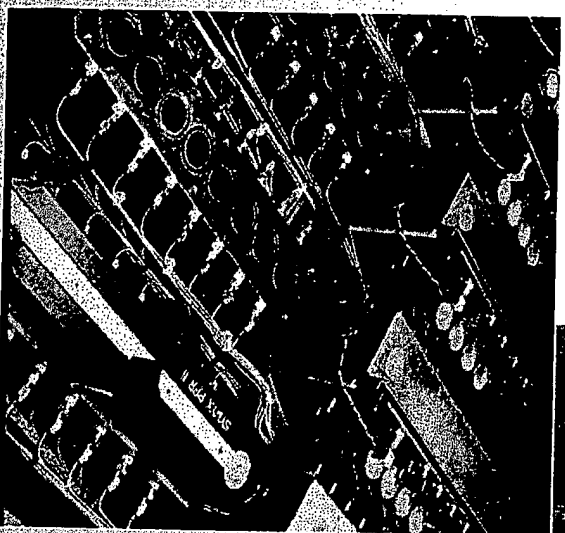
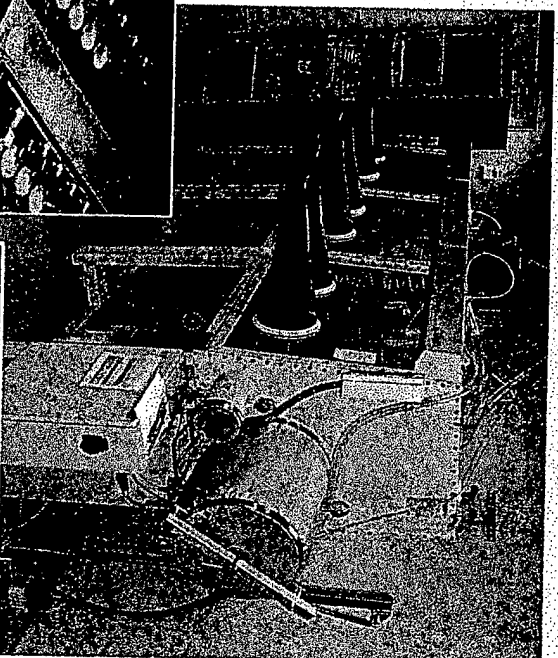
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Secondary Screening Tools

Symyx Parallel Polymerization Reactor (PPR®)



- 48 reactions per run
- 6 mL reaction volume
- Reagents injected robotically at T and P
- Real-time monitoring
 - T, P and gas uptake in cell



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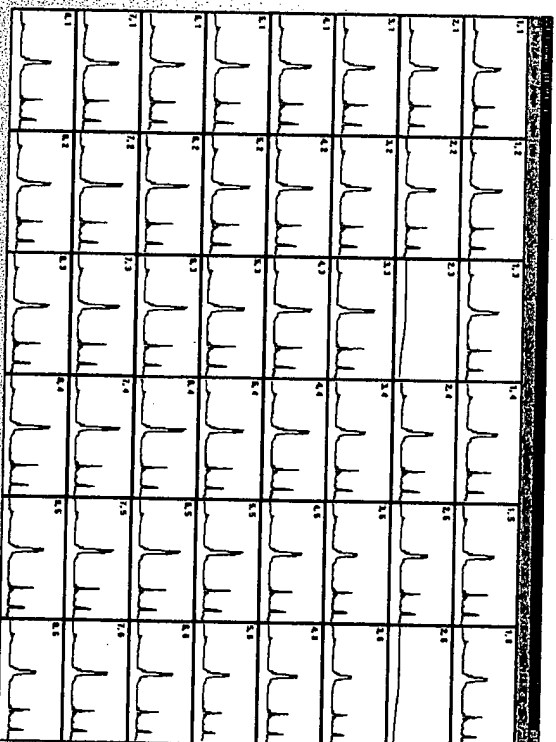
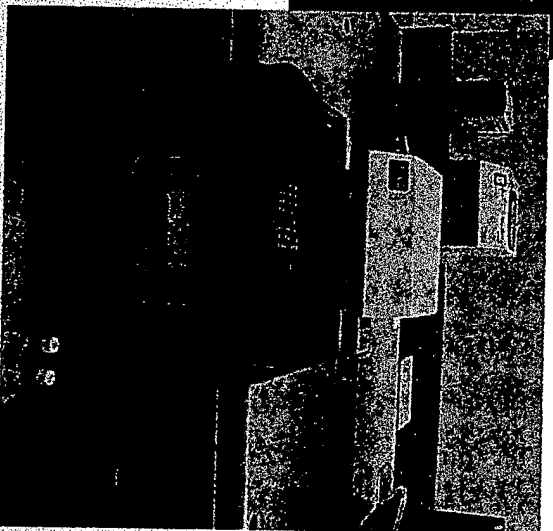
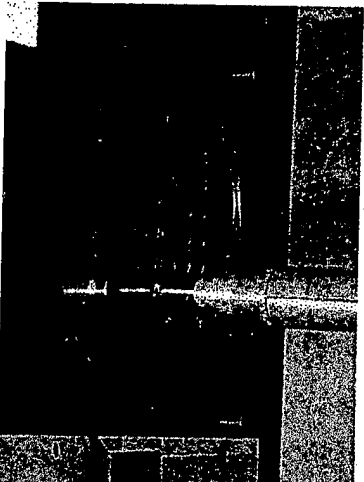
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Secondary Screening Analysis: FT-IR



IR spectra of polymers allows rapid analysis of:

- co-monomer composition
- tacticity



Automated Reflection FT-IR Analysis of Polymer Films

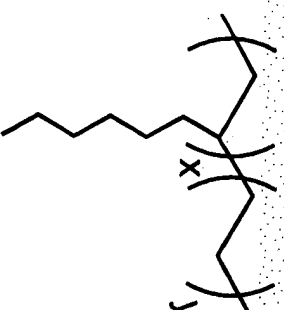
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A Case Study of High-Throughput Catalyst Discovery

Target: High Temperature Solution Phase LLDPE Catalyst

- ❖ Catalyst must operate at temperatures $> 130^{\circ}\text{C}$
- ❖ Requires high activity, high M_w , high 1-octene incorporation



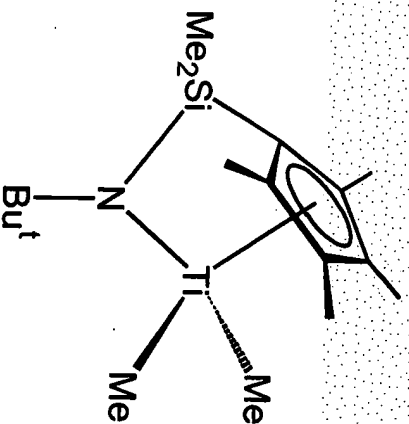
Primary Screen:
1-Octene Polymerization Activity

Hits and Information

1-Octene Polymerization Capability

Secondary Screen:
High Temperature Ethylene/ 1-Octene Screen

Adaption to Small Scale: Primary Screening Validation



1 ml Glass Vials

Monomer: 120 μ l 1-Octene

Total Volume: 220 μ l (toluene)



[8 x 12] Array

3 Catalyst Concentrations

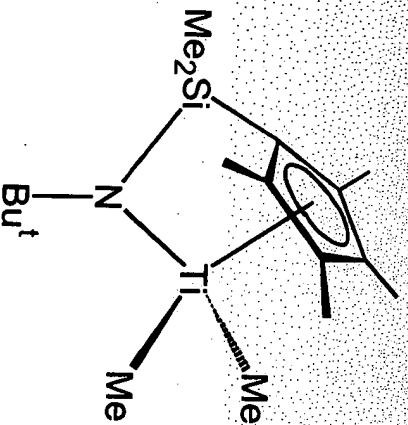
4 Activation Methods

8 Replicates of Each

Condition

Use robots to dispense reagents and to analyze products for speed, accuracy

Adaption to Small Scale: Primary Screening Validation

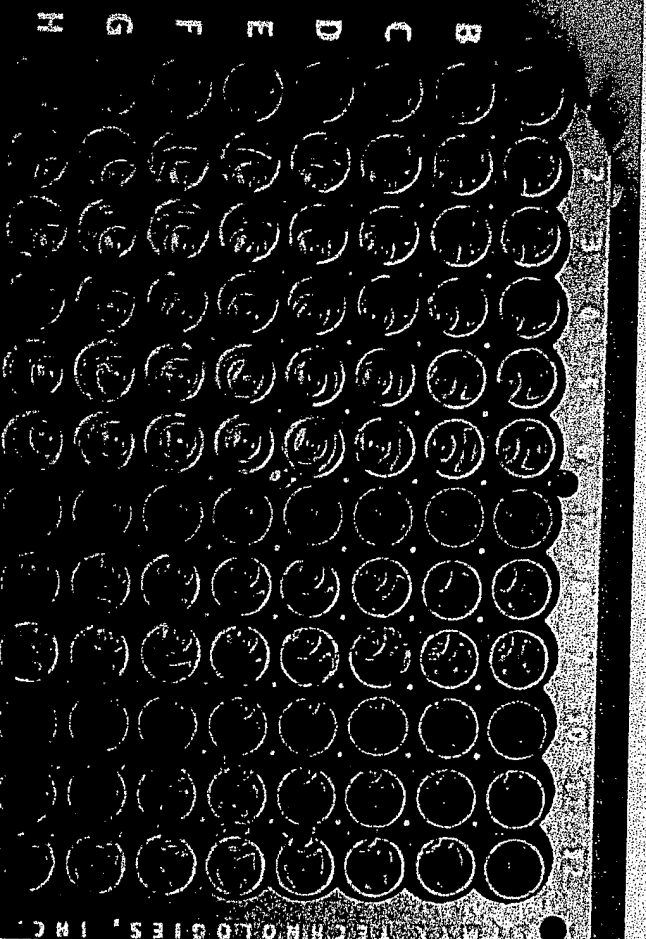


Monomer: 120 μ l 1-Octene
Total Volume: 220 μ l (toluene)

Column No.

4 Activation Zones

3 Catalyst Concentrations (mM)



SMX-10000-1 REV.A

SPACING = 9 MM (0.3543 IN)

1	2	3	4	5	6	7	8	9	10	11	12
None (Control)			200 eq. MAO			[Me ₂ PhNH] ⁺ [B(C ₆ F ₅) ₄] ⁻			[Me ₂ PhNH] ⁺ [B(C ₆ F ₅) ₄] ⁻ + 5 eq. Bu ₃ Al		
1.8	0.18	0.018	1.8	0.18	0.018	1.8	0.18	0.018	1.8	0.18	0.018

DOW

8 Replicates



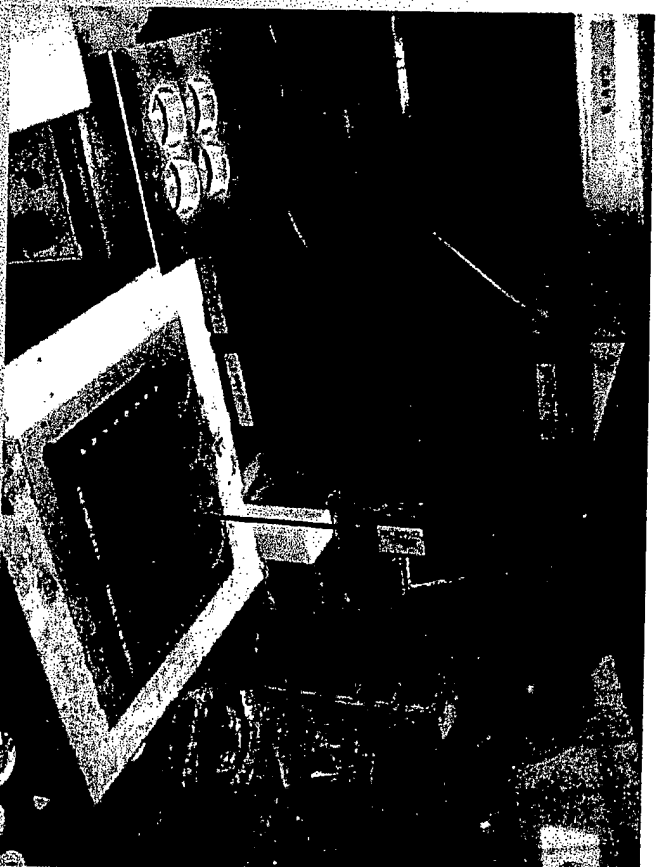
Adaption to Small Scale: Primary Screening Validation Procedure

1. Add 120 μL 1-Octene.
2. Add Bu^i_3Al to columns 10, 11, 12.
3. Add $[(\eta^5\text{-C}_5\text{Me}_4)\text{SiMe}_2(\eta^1\text{-NBu}^i)\text{TiMe}_2]$.
4. Add Activators.



1. Run Polymerization
2. Quench, Filter
3. Automated Dilution
4. Rapid GPC™
5. Obtain M_w , Conversion

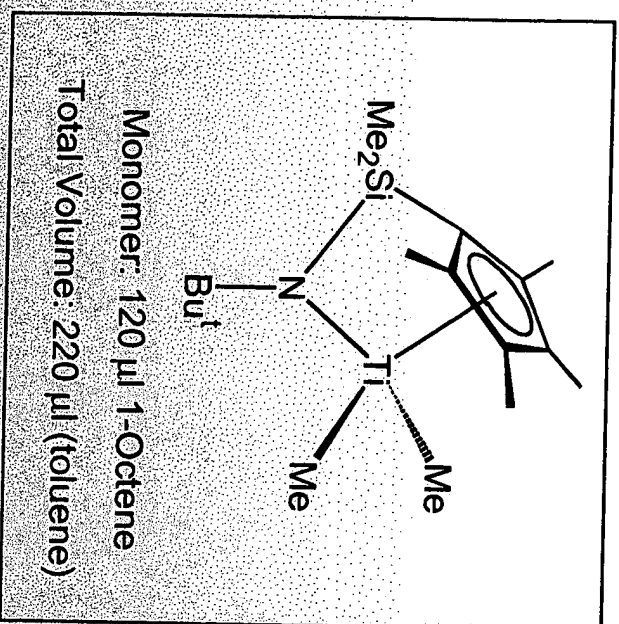
All Procedures Employ
Robotic Liquid Handling



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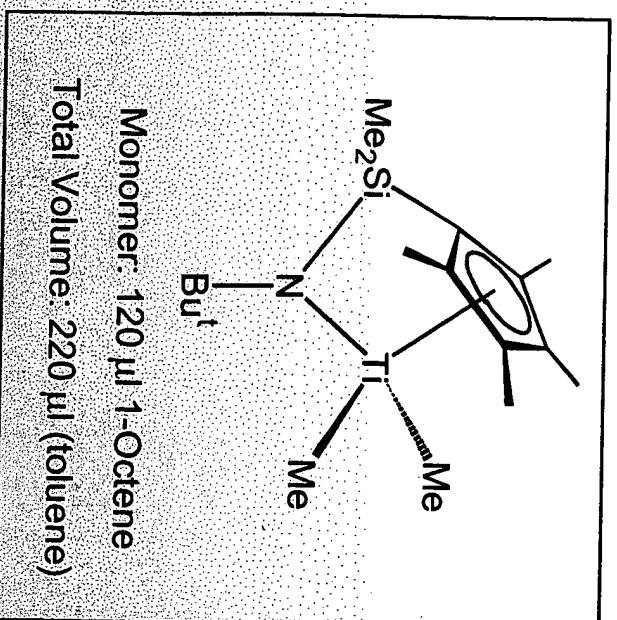
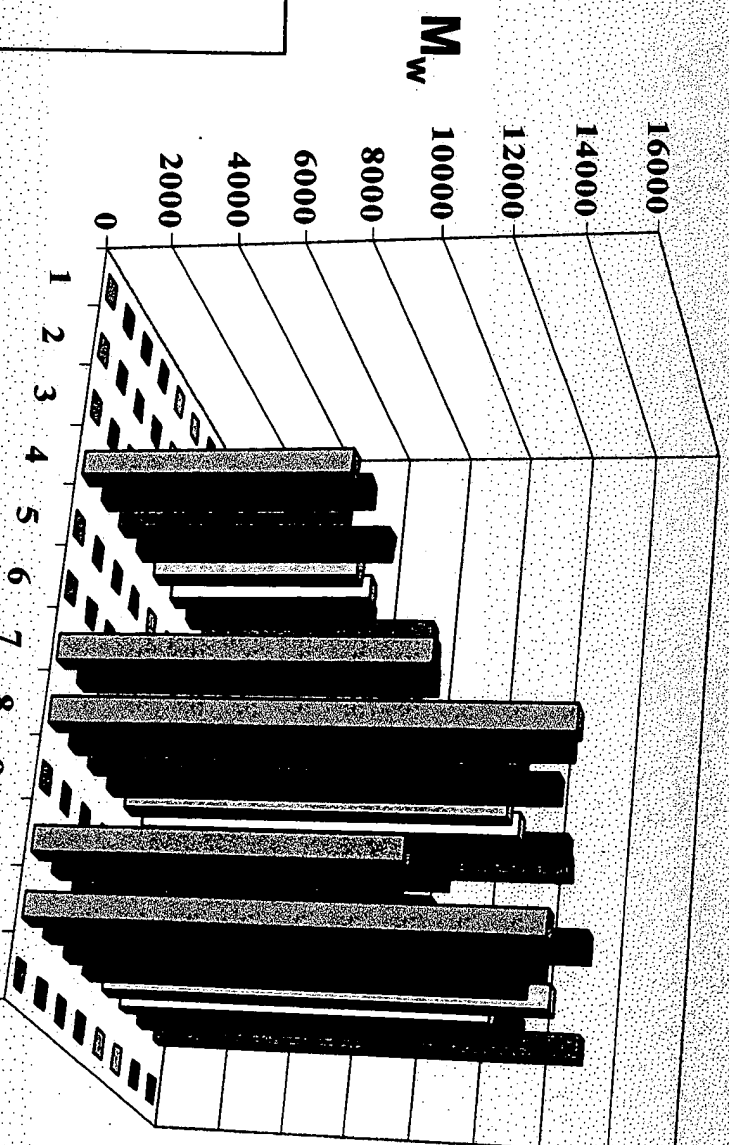
DOW

% Conversion to Poly-1-Octene



3 Catalyst Concentrations (mM)

Adaption to Small Scale: Primary Screening Mw Validation



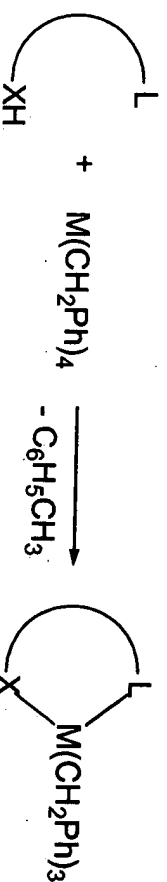
None			200 eq. MAO			[Me ₂ PnNH] ⁺ [B(C ₆ F ₅) ₄] ⁻			[Me ₂ PnNH] ⁺ [B(C ₆ F ₅) ₄] ⁻ + 5 eq. Bu ₃ Al		
1.8	0.18	0.018	1.8	0.18	0.018	1.8	0.18	0.018	1.8	0.18	0.018

3 Catalyst
 Concentrations
 (mM)

Catalyst Discovery Screening

- Adaption of the Chemistry to Smaller Scale
- Large Number of Ligands with Suitable Diversity
- Efficient Methods of Attaching Ligands to Metals
- Suitable Rapid Screening Technique

The Use of Acidic ligands with $M(\text{CH}_2\text{Ph})_4$ ($M = \text{Zr}, \text{Hf}$) and Multiple Activation Conditions



[3 x 8] Set of
Charged Ligands

$M(\text{CH}_2\text{Ph})_4$
($M = \text{Zr}, \text{Hf}$)

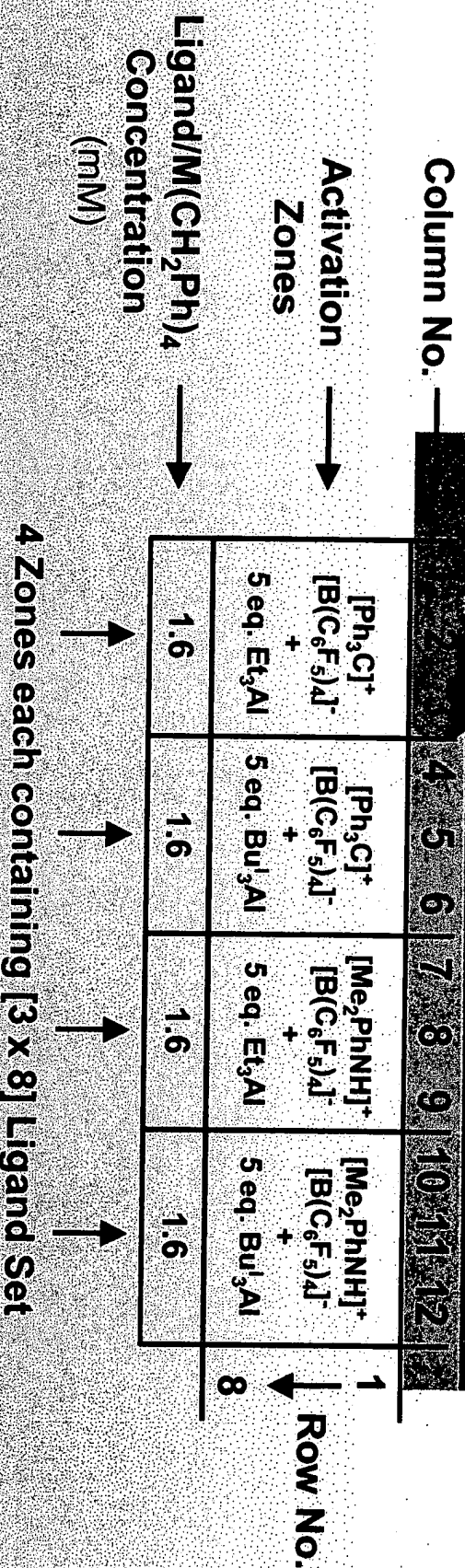
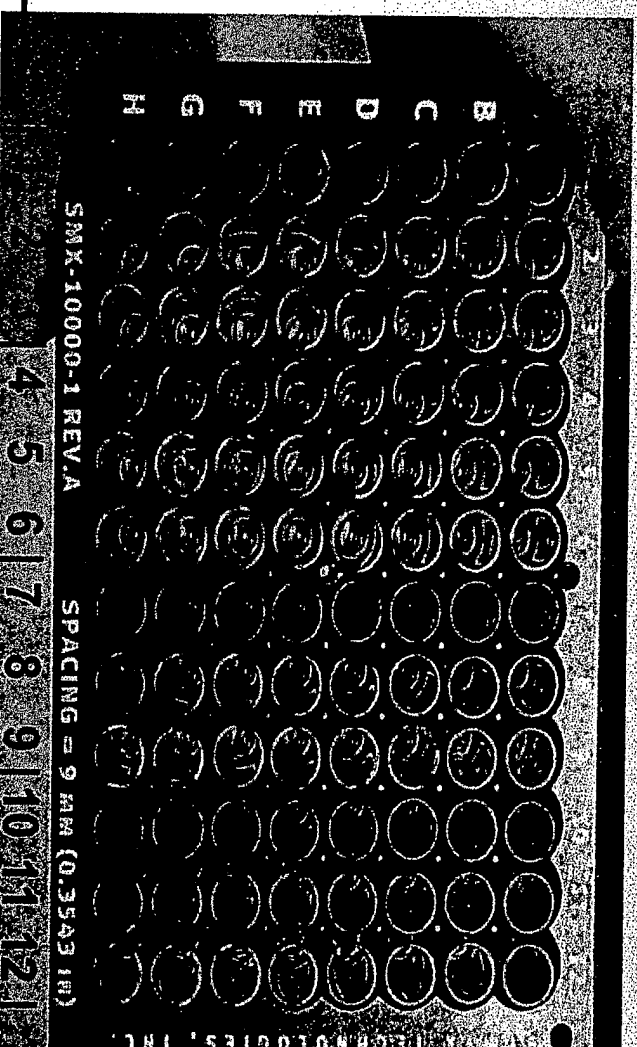
1 Hour, Toluene

Ligand/ $M(\text{CH}_2\text{Ph})_4$
Mixtures

Multiple Activation
Conditions

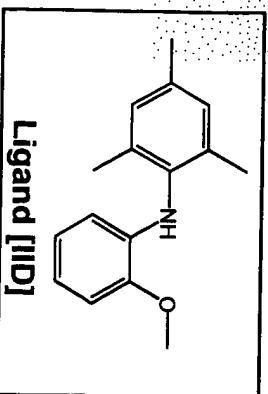
Catalyst Discovery Screening - Plate Design

Discovery Plate Design
Eight Activation
 Conditions for Each
 Ligand/ $M(CH_2Ph)_4$
 Combination
 - 2 plates of 4
 conditions

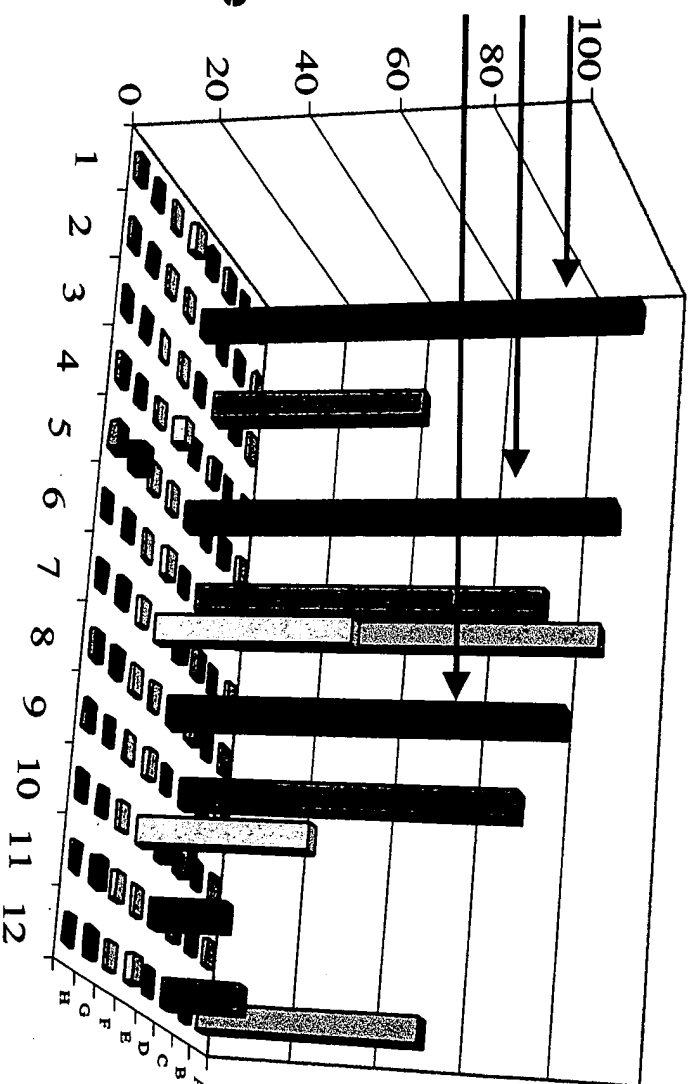


Catalyst Discovery Screening - Activity Results

% Conversion Data



% Conversion
to Poly-1-Octene



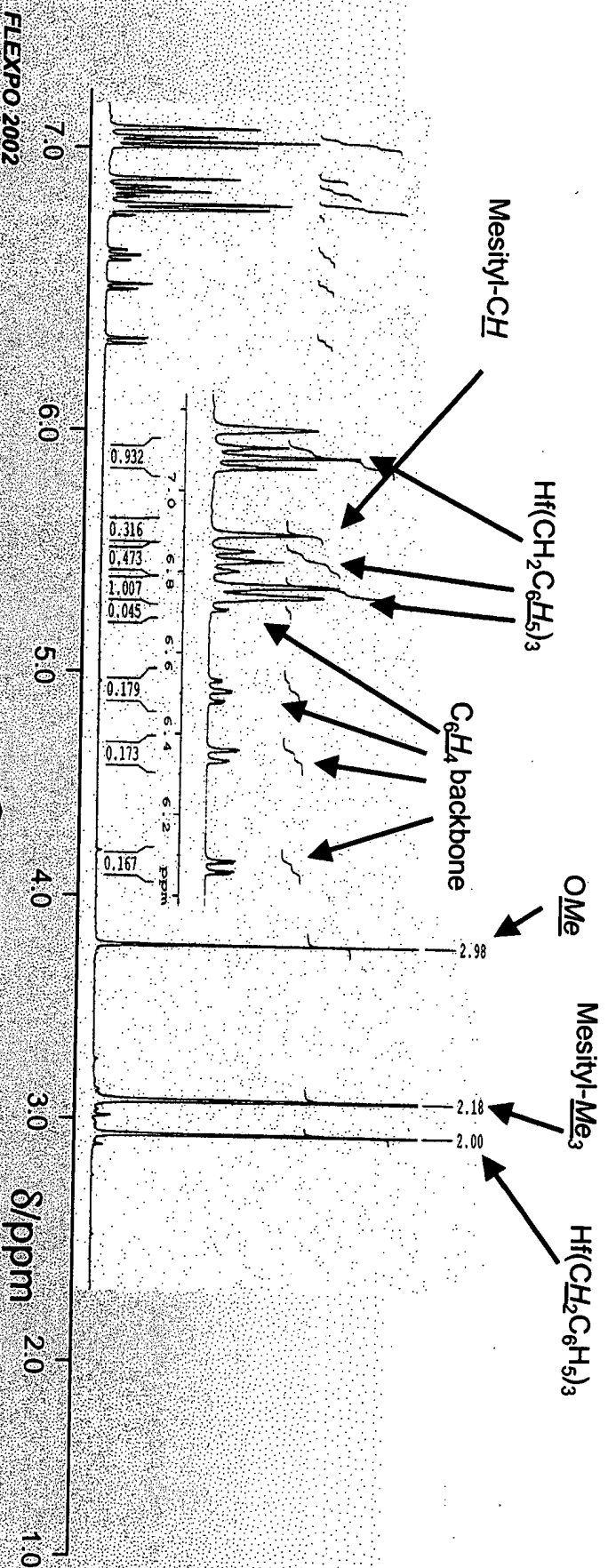
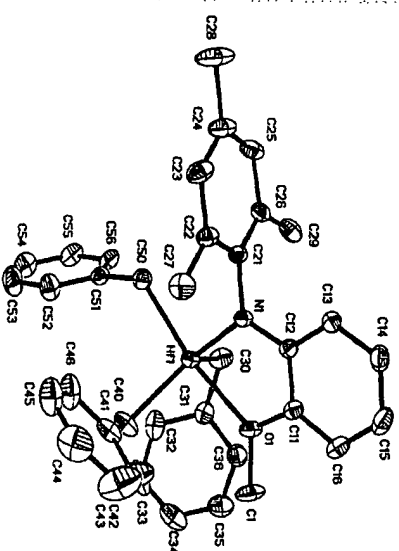
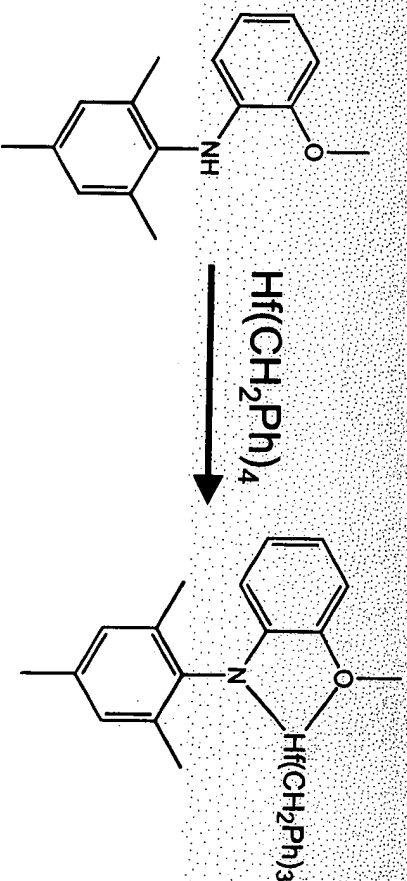
Ligand/ $\text{Hf}(\text{CH}_2\text{Ph})_4$
Concentration
(mM) \longrightarrow

$[\text{Me}_2\text{PhNH}]^+$ $[\text{B}(\text{C}_6\text{F}_5)_3]^-$ + 5 eq. Et_3Al	$[\text{Me}_2\text{PhNH}]^+$ $[\text{B}(\text{C}_6\text{F}_5)_3]^-$ + 5 eq. Bu_3Al	$[\text{Ph}_3\text{C}]^+$ $[\text{B}(\text{C}_6\text{F}_5)_3]^-$ + 5 eq. Et_3Al	$[\text{Ph}_3\text{C}]^+$ $[\text{B}(\text{C}_6\text{F}_5)_3]^-$ + 5 eq. Bu_3Al
1.6	1.6	1.6	1.6

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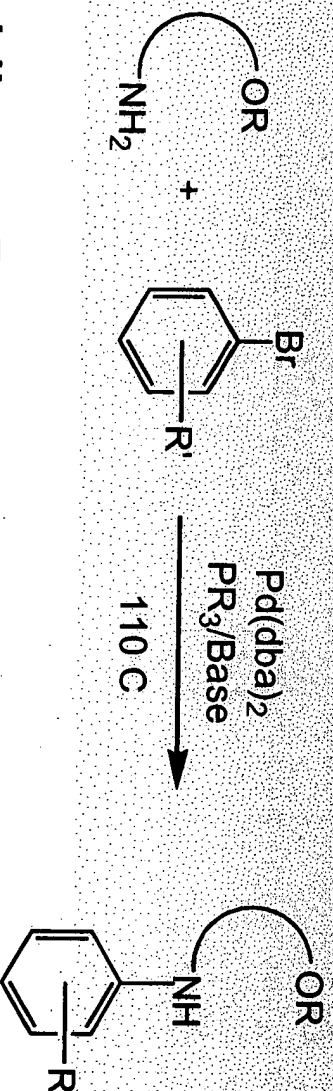
After Hit Identification, Conventional Chemistry Identifies Structure of Active Catalyst



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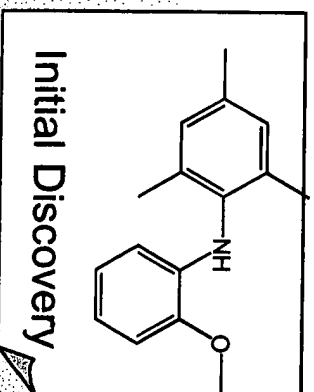
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Focus Library of Structural Variation Around Identified Hit

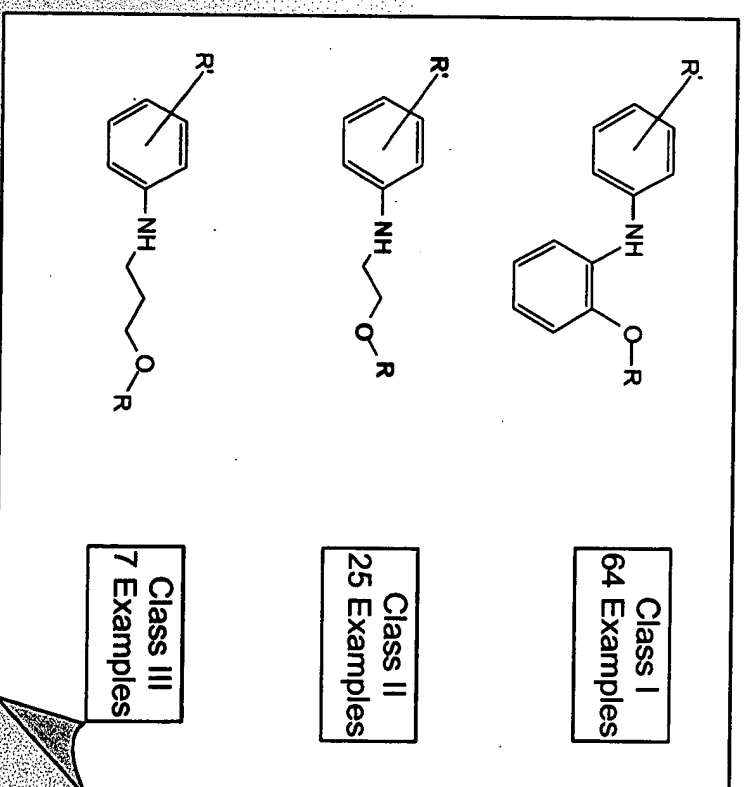


Focus Library Preparation

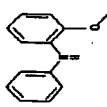
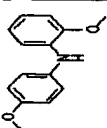
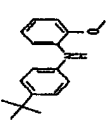
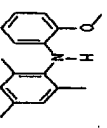
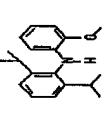
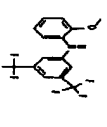
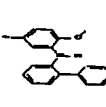
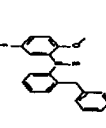
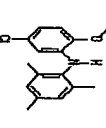
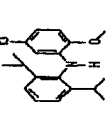
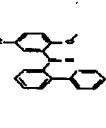
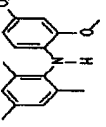
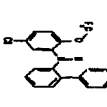
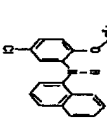
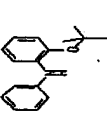
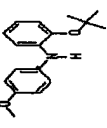
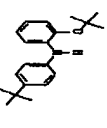
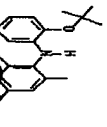
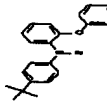
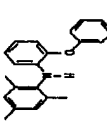
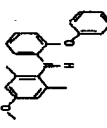
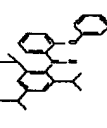
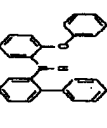
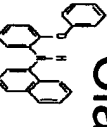
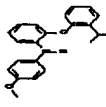
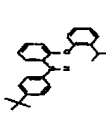
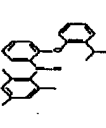
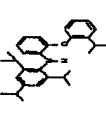
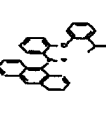
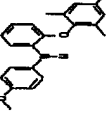
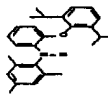
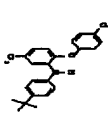
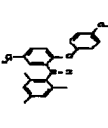
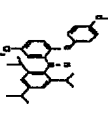


❖ 96 Structural Variations






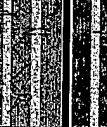






Robotic synthesizers used to produce library



Focus Library for Amine Ether Hit

Class 1

Class 3

Secondary Screening

96 High Temperature Ethylene-Octene Copolymerizations

Reactor Conditions
130 °C, 100 psi Ethylene
6.1 mL Total (Toluene)
0.25 mL 1-Octene
2 μmol Bu^i_3Al
1 μmol $\text{Hf}(\text{CH}_2\text{C}_6\text{H}_5)_4/\text{Ligand}$

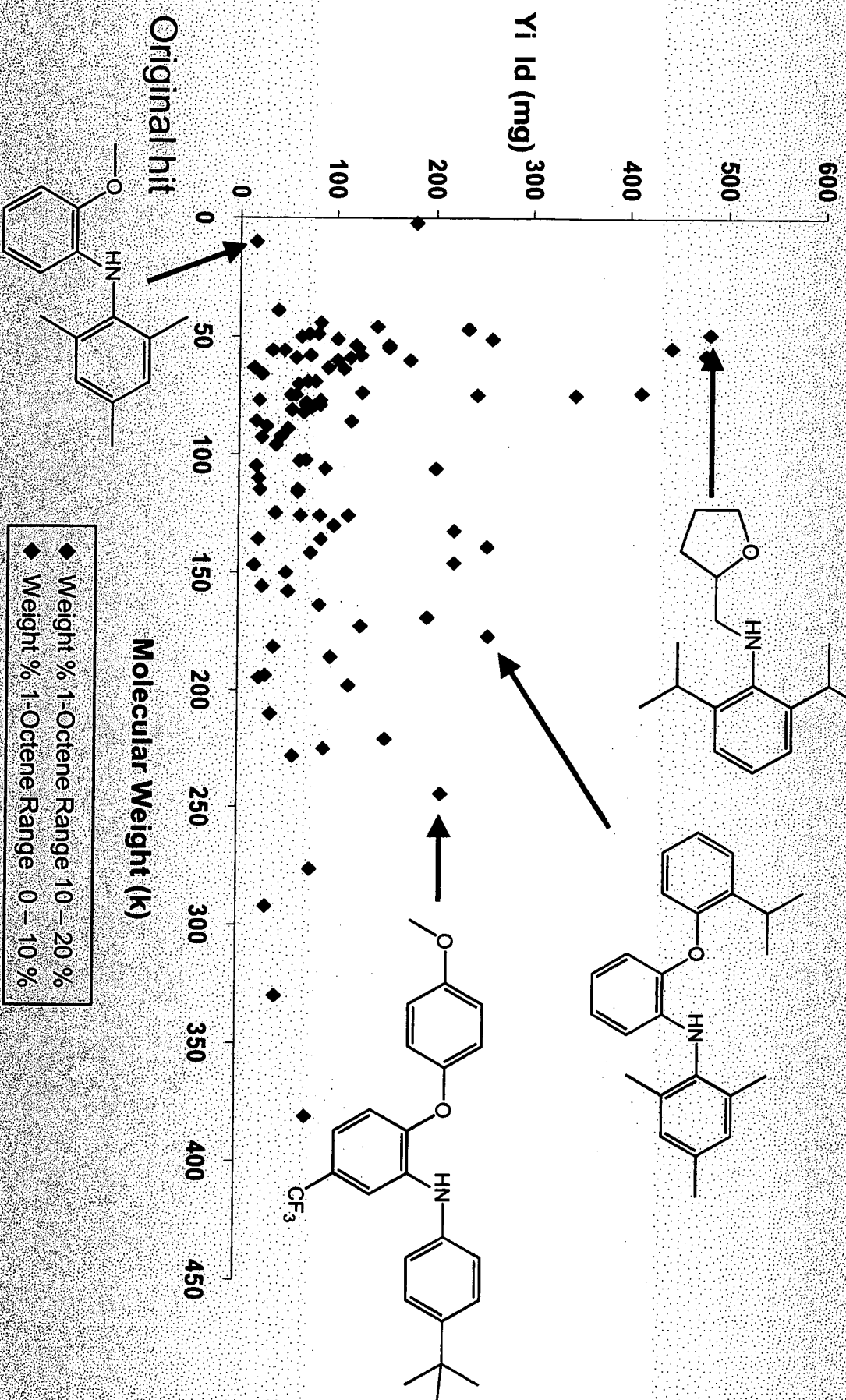


Target:
200-300 mg Copolymer

[8 x 12] Ligand Set

$\text{Hf}(\text{CH}_2\text{Ph})_4$	1) Add Bu^i_3Al	
$\xrightarrow{1 \text{ Hour, Toluene}}$	2) Add $[\text{Me}_2\text{PhNH}][\text{B}(\text{C}_6\text{F}_5)_4]$	
	$\xrightarrow{}$	Obtain yield, molecular weight, MWD, wt. % 1-octene
	3) Inject Ligand/ $\text{Hf}(\text{CH}_2\text{Ph})_4$	
	4) Monitor Run for 30 Minutes	

Focus Library Identifies Large Structure / Activity Effects in this Family, Improved Catalysts

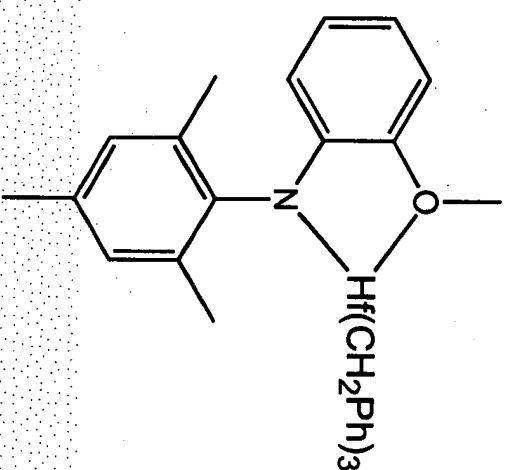
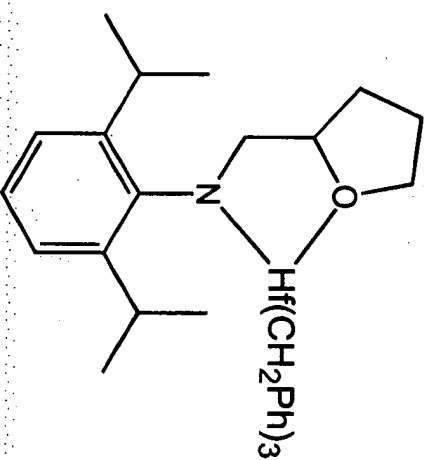


FLEXPO 2002



1 Gallon Industrial Ethylene 1-Octene Autoclave Results Using Isolated Catalysts Validate Screening Results

Performed in Solution
Phase
at 130 °C



Activity (g poly/mmol Hf)	13,760	7,560
M_w	181 k	97 k
M_w/M_n	2.8	3.0
Density	0.917	0.910

Conclusions

Effective high-throughput combinatorial methods have been developed for organometallic polyolefin catalyst systems

Months or years of conventional catalyst research can be accomplished in days or weeks

Small-scale 1-octene polymerization screens were validated using a commercial catalyst

New hafnium post-metallocene catalyst family was discovered

Focus library of 96 structural variations was rapidly investigated

- significant enhancements observed
- wide variation in structure / property response

Optimized structures scaled up to commercial-scale process reactors